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APR 20 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20857

Re: Docket No. 98D-1267
Guidance for Industry "NDAs: Impurities in Drug Substances" - Draft Guidance

Dear Sir/Madam:

Reference is made to the above-noted Draft Guidance originally published in the Federal Register on 21 January 1999, Docket Number 98D-1267.

At this time, on behalf of The R.W. Johnson Pharmaceutical Research Institute (RWJPRI), we wish to provide our comments to this Draft Guidance. Our comments are both General and specific and are identified as such.

We greatly appreciate the opportunity to comment on this document and look forward to similar opportunities in the future.

Very truly yours,

Donna Panasewicz
Director
Regulatory Affairs

Attachment

98D-1267

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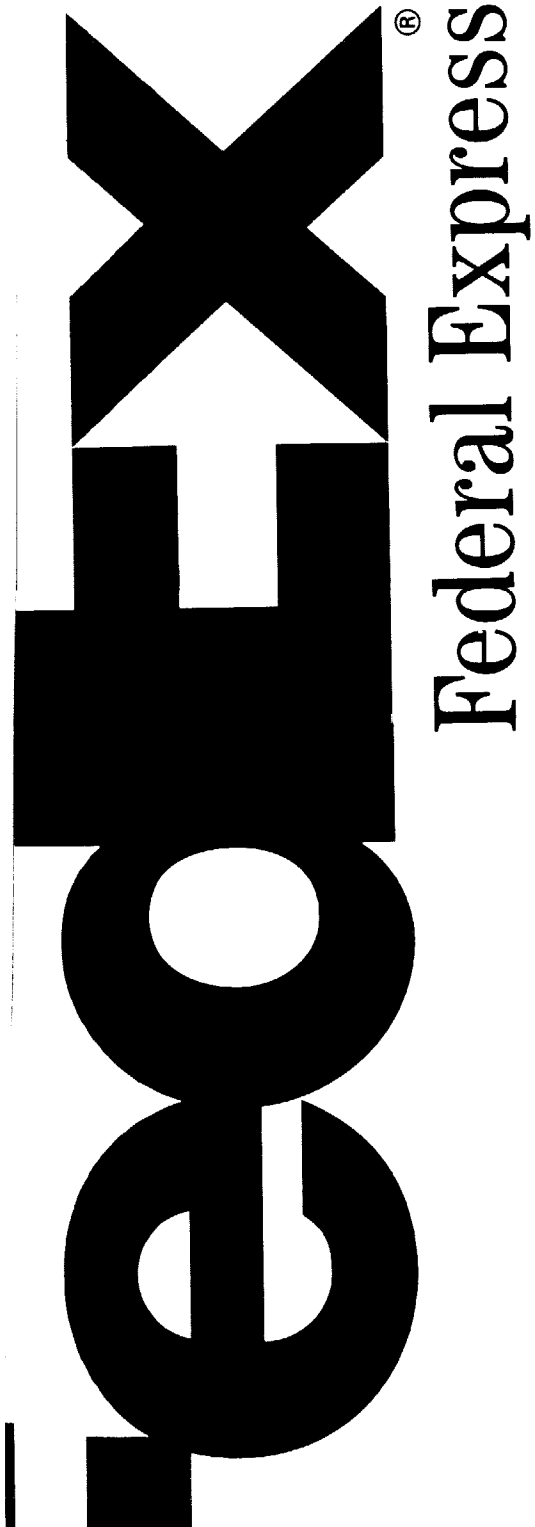
The following comments and suggestions are being respectfully submitted in response to the issuance of the Draft Guidance for Industry on NDAs: Impurities in Drug Substances.

General Comments:

It is our company's opinion that the Agency has varied from ICH Q3A in that the guidance requires reevaluating impurity information for sNDA and line extensions, whereas ICH states "This document is intended to provide guidance...impurities in new drug substances produced by chemical syntheses and **not previously registered** in a region or member state." The Agency has stated that this guidance document includes "Examples of NDAs affected by the recommendation including those submitted for new dosage forms of **already approved drug products**, or drug products containing two or more active moieties that are individually used in **already approved drug products** but have not previously been approved or marketed together in a drug product." It is our company's position that this difference from the ICH is appropriate only when a method to detect impurities is currently not references in the drug substance specifications.

Specific Comments:

- Section Titled "Supplemental Information" first paragraph, referring that this guidance also "applies to drug substances...not considered new drug substances." Our concern is that this could potentially create a process that would slow down a regulatory filing unnecessarily.
- Section 3.1 "Organic impurities" and Section 4. "Analytical Procedure". Clarification is needed in that for an sNDA where there is no synthesis change and the specification contains an impurity method, there is no need for a new tabulation of impurity data. For an sNDA containing no impurity method, or for a compendial item without a purity method, an additional method should be developed and a tabulation of impurity data obtained.
- Section 5. "Reporting Impurity Content of Batches". We agree that the data should be available but not necessarily be filed as part of the new NDA when the drug substance sections are being cross-references to a previous NDA. For an sNDA or for an NDA where the drug substance specification contains a purity method and there is no change in the synthesis method, there is no need for data to be tabulated in the submission since data will be available in the batch records.
- Section 6. "Specification Limits for Impurities" The last paragraph which refers to mass balance and analytical error should be deleted. This paragraph adds nothing to this section and is stating the obvious. With drug substance specifications for assay typically being 98.0-102.0%, this paragraph becomes unnecessary to state in this guidance.



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